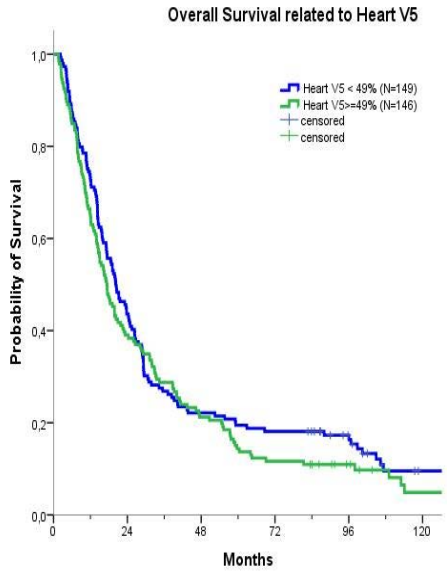
Table 1		Median	Range	SD
Age (year)		67	34-88	9.29
Heart V_5 (%)		49	0-100	1.83
Mean heart dose (Gy)		14	0.1-47.5	11.4
Follow up (month)		127	81-168	25.7
			N=295	(%)
Gender	Female		118	40
	Male		177	60
Performance status	0-1		239	81
	>1		56	19
Smoking	Yes*		246	83
	No#		49	17
Histology	Sq. cell carcinoma		146	50
	Adeno carcinoma		104	35
	Other		45	15
Dose (Gy)	60		193	65
	66		90	31
	80		12	4
Concomitant chemotherapy			34	12

* Current or ex-smoker within 10 yr. # Never or ex-smoker at least for 10 yr.



Conclusion: This study did not show that heart V5 or MHD had a negative effect on survival for NSCLC patients treated with definitive radiotherapy. This study differs from recently reports by having a longer follow-up. On the other hand, concomitant chemotherapy was only used in 12% of the patients in this study. The main goal for NSCLC patients is still to achieve better loco-regional control. However, if dose escalation is performed with doses significant above those in the present study, strict dose constraints to the heart might still be advisable based on experience from patients with breast cancer.

PO-0685

Is PET imaging a reliable target for dose painting by numbers in lung cancer?

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Purpose or Objective: Since many years, PET has been foreseen as a promising candidate for dose painting. However, the lack of biological specificity of tracers together with the low spatial resolution could call PET into question as a reliable target for voxel-based dose prescription.

To address this issue, we analysed FDG (tumor burden) and FAZA (hypoxia) PET uptake distributions in lung tumours in terms of biological specificity, spatial resolution, and spatiotemporal evolution.

Material and Methods: Twelve patients with locally advanced lung carcinomas treated by concomitant chemo-radiation were prospectively included. These patients underwent 4D PET/CT (FDG and FAZA) with audio coaching at 3 time-points: prior to radiotherapy, and in the second and the third weeks of treatment. All images were reconstructed in their time-weighted mid-position (MidP).

At each time-point, CT-based rigid registration was performed between FDG and FAZA MidP PET/CT while CT-based deformable registration was performed between per- and pre-treatment images.

In order to be compared with native FDG images, simulated PET images (PETsim) were created. To this end, tumours were segmented on FDG images (GTVFDG) using a gradient-based method relying on watershed and clustering. Subsequently, binary images were generated (uniform activity inside and null activity outside GTVFDG) and blurred using a Gaussian kernel of 8-mm FWHM.

PET SUV within the GTV were pairwise compared on a voxel-by-voxel basis using Spearman's correlation (rs) between:

- FDG and FAZA images, to assess their respective specificity
- FDG and PETsim images, to assess to which extent the blurring effect linked to the limited spatial resolution impacts the observed tracer distribution)
- per- and pre-treatment images, to assess the spatiotemporal evolution of the uptake distribution during radiation therapy

Results: At each time point, FDG and FAZA SUVpeak showed high correlation (r = 0.78) (Fig. 1A). FDG and FAZA voxel-by-voxel comparison showed high correlation (rs = 0.75 ± 0.13). This correlation was even higher when the 50% more hypoxic tumours were considered (FAZA SUVpeak = 1.83 ± 0.32 ; rs = 0.80 ± 0.05), compared to the 50% less hypoxic (FAZA SUVpeak = 1.17 ± 0.22 ; rs = 0.69 ± 0.16) (Fig. 1B).

Similarly, high correlation was found between FDG and PETsim images (rs = 0.78 ± 0.14).

Finally, the uptake distribution was spatially stable through imaging sessions for both tracers (FDG: rs = 0.86 ± 0.09; FAZA: rs = 0.82 ± 0.11).

All results were significant (p < 0.01).

Fig 1a. Comparison between FDG and FAZA SUV_{peak}
FDG and FAZA SUV_{peak} showed high correlation (r = 0.78).

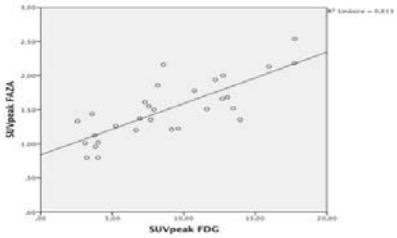
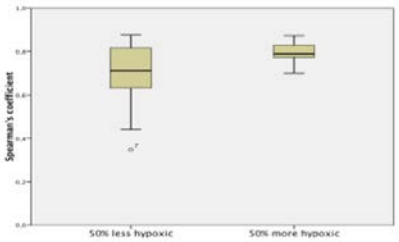


Fig 1b. Voxel-based comparison between FDG and FAZA SUV
FDG and FAZA voxel-by-voxel comparison showed high correlation (r_s = 0.75 ± 0.13). The correlation was higher for the 50% more hypoxic tumors (r_s = 0.80 ± 0.05) than for the 50% less hypoxic (r_s = 0.69 ± 0.16).



Conclusion: FDG and FAZA PET images share similar uptake patterns, even more for hypoxic tumours. In addition, FDG and FAZA uptake distribution were stable over treatment time. Blurring caused by the limited spatial resolution seems to be the main driver of the observed uptake distributions, as

suggested by the comparison between real and simulated images.
These results question the use of PET imaging as a target for dose painting by numbers in lung cancer.

PO-0686
Locoregional failure in locally advanced non-small cell lung cancer after definitive radiotherapy
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Purpose or Objective: To determine the patterns of locoregional failure (LRF) in patients with locally advanced non-small cell lung cancer treated with definitive radiotherapy (RT).

Material and Methods: One hundred and fifty-four patients from the Gating 2006 prospective randomized trial (NCT00349102) were treated with conformal RT with or without respiratory motion management. All patients had a PET-CT with 18FDG in the two months leading up to study inclusion. The recommended protocol prescription was 66 Gy in daily 2-Gy fractions, five days a week. IMRT was not permitted. Patients with a LRF as first event were included. Treatment plannings with simulation CT, pre-treatment 18FDG PET-CT and post-treatment images demonstrating recurrence were registered and analyzed. Measurable LRF was contoured (rGTV) and classified as in-field (if 95% of rGTV volume was within the 95% isodose), marginal (if 20 to 95% of rGTV volume was within the 95% isodose), or out-of-field (if less than 20% of rGTV volume was within the 95% isodose).

Results: Median follow-up was 27.8 months. Forty-eight patients presented LRF. One-year and 2-year locoregional disease-free survival were 77% (95% CI 70-83) and 72% (95% CI 64-79) respectively. Age was the only independent LRF prognostic factor. The median age for patients in LRF was 67 years vs 60 years for the group not in LRF (p=0.009). 79% of the patients with LRF as first event relapsed within the RT field. 32% of patients with LRF had a marginal LRF component. Isolated out-of-field failure occurred in only 3% of all patients. The regions of highest FDG-uptake on pre-treatment PET-CT were located within the recurrence in 91% of patients with in-field LRF.

Conclusion: In-field failure was the most common pattern of failure. Escalated dose RT with high-dose fractions guided by PET parameters warrants further investigation.

PO-0687
Machine learning method for biomarkers identification in lung cancer patients
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Purpose or Objective: Treatment of lung cancer (LC) with radiotherapy (RT) is often accompanied by the development of relapse. The significance of biologic markers for predicting recurrence has been increasingly emphasized by recent studies. Highly accurate and reliable machine-learning approaches can drive the success of biomarkers identification in clinical care. We developed a prospective platform to incorporate translational research into the clinical decision making process in LC patients.

Material and Methods: Prospective data from 138 consecutive LC patients with indication of radio(chemo)therapy and diagnosis from January 2013 to August 2014 were available to enable the development of a prediction model. Median age was 62.5 years-old (range, 35-88) and the Karnofsky performance status (KPS) was ≥70 except for 129 cases. The most common histology for non-small cell LC patients (77.5%) was squamous cell carcinoma (52.3%). 73.1 percent of patients had Stage III disease (9 cases were a mediastinum recurrence) and 91 % received platinum-based chemotherapy. Median total dose prescribed was 61.2 Gy. 20 cases also underwent surgery. Data from translational research included genotypes of 4 single nucleotide polymorphisms (SNPs) of the transforming growth factor (TGFB1) gene (rs4803455, rs1800468, rs8179181, and rs8110090) and 3 SNPs of the heat shock protein (HSPB1) gene (rs2868370, rs2868371, and rs7459185).

Results: In univariate analysis, the CA genotype (N=92; 64 relapses [70%]) of TGFB1 rs4803455 was associated with a statistically significantly higher risk of recurrence (OR = 2.09; P = 0.045) compared with the CC genotype (N=46; 24 relapses [52%]). This effect was virtually unchanged after multivariate analysis (OR = 2.31; 95% CI, 1.08– 4.95; P = 0.031). In addition, we performed an ROC curve analysis to determine the strength of the above identified biomarker in predicting relapse. Age was the most important predictor, with an AUC of 0.62. By adding the TGFB1 rs4803455 SNP, the predictive power of the recurrence risk model improved, enhancing the AUC to 0.67 (95% CI, 0.57– 0.76; P = 0.001).

Conclusion: The prediction model for recurrence of patients with LC highlights the importance of combining patient, clinical, treatment, and translational variables. Our results showed that the CA genotype of TGFB1 rs4803455 SNP was associated with a higher risk of relapse in patients with LC treated with radio(chemo)therapy and thus may be used for guiding therapy intensity or as a selection criteria for a clinical trial, which would further the goal of individualized therapy. This tool could be used as a first building block for a decision support system.

PO-0688
Patterns of LR for stage III N2 NSCLC patients after chemotherapy and surgery: implications for PORT
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Purpose or Objective: To evaluate loco-regional patterns of failure after induction chemotherapy and surgical resection for stage III N2 non-small-cell lung cancer (NSCLC).